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Cost-effectiveness analysis of a cervical cancer vaccine in five Latin American countries

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ABSTRACT

Implementation of cervical cancer (CC) vaccination in Latin America is expected to reduce the high CC burden in those countries. But the efficiency of such vaccination programs in the region still remains unknown. This study assesses the cost-effectiveness and cost-utility of introducing vaccination into the current CC disease management of five Latin American countries (Argentina, Brazil, Chile, Mexico, and Peru). The modelling results indicate that universal mass vaccination is cost-effective in the current health care setting of each country (<3× gross domestic product per capita, per country) with a substantial number of CC cases and deaths avoided in addition to an increase of quality-adjusted life years. This study will help guide the design of future clinical programmes and health-related policies. It will assist early and effective decision-making processes related to vaccine implementation in Latin America.

1. Introduction

Human papillomavirus (HPV) commonly infects the genital mucosa of sexually active women and is associated with the later development of cervical cancer (CC) [1,2]. The distribution of HPV types differs by geographic region. Overall, HPV types 16 and 18 have been shown to be the causative agents in approximately 70% of detected CC cases [2]. The eight most common genotypes (HPV 16, 18, 45, 31, 33, 52, 58 and 35) account for more than 90% of all CC cases [3–5].

CC is the third most common cancer in women worldwide after breast and lung cancer [6]. It represents a major social and economic burden affecting relatively young women of productive and reproductive age. About 83% of the CC cases occur in developing countries and this figure is expected to increase to 90% by the year 2020 [7]. It is currently also one of the leading causes of cancer death in developing countries. In Latin America and the Caribbean, CC contributes to more life years lost (LYL) than tuberculosis, maternal conditions or AIDS [8]. An estimate from GLOBOCAN statistics shows a total of 71,862 newly diagnosed cases and a total of 32,639 deaths reported for the year 2002 in this region [6].

The incidence and mortality of CC have declined during the last decades in many developed countries, mainly due to the improving socio-economic levels and to the implementation of screening and early treatment programmes with a sufficiently wide coverage [9]. However, incidence and mortality rates have remained relatively stable in developing countries. This may be due to the difficulties of implementing screening programmes with high population coverage and good quality control of cytology [7,10,11]. In particular, Latin America still has a high incidence and mortality rate of CC because of both the high frequency of risk factors and the low screening coverage [12]. But both elements vary widely across the countries in the region.

Two different vaccines against oncogenic HPV 16/18 have recently been introduced to the market [13–16]. Both vaccines are recommended for girls between 10 and 12 years. In general, vaccination offers protection against specific HPV infection, and subsequently the development of pre-malignant and malignant lesions. Vaccination is an easier prevention measure than any other preventative intervention [17,18]. The implementation of CC vaccination may have a significant impact on low and middle-income countries where health care resources are limited. Multiple fac-

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tors should be analyzed such as disease burden, effectiveness of the intervention, the budget required to initiate and sustain the program, the cost-effectiveness of the intervention, the infrastructure necessary to successfully deliver the intervention, and the likelihood of cultural acceptability, political will and public sector support [19,20]. Also, important questions are emerging about how the investment in a vaccine program will compare with the newly proposed screening strategy that applies cytological screening only 3 times in a woman's life between the age of 35 and 45 years [21].

Cost-effectiveness analysis is a useful tool to assist decision makers in allocating resources and effectively implementing a specific health-related intervention. Several models have been developed to assess the cost-effectiveness of existing and new interventions which reduce HPV-associated pre-cancerous and cancerous lesions [17,18,22–26]. These models compare different scenarios such as screening strategies for the early detection of CC and vaccination against HPV types 16 and 18, among others. The modelling results vary widely from one country to another due to differences in cultures and regions related to the level of acceptance of specific interventions, the incidence of certain pathologies, treatment-related costs, etc. Country-specific assessment therefore needs to be conducted in order to suitably inform local decision makers.

We performed a cost-effectiveness and cost-utility analysis regarding the introduction of vaccination in a population with a high CC disease burden in Argentina, Brazil, Chile, Mexico and Peru. The selected five Latin American countries show very different approaches in their health care system, have different CC morbidity/mortality rates and varied success in CC prevention. A high proportion of women in the region have never had a Pap smear, and these women are in general at increased risk of CC [12]. Chile had the greatest impact of its screening programs during the last few years, showing a 162% increase in Pap smear coverage between 1987 and 2003, and a 39% decrease in CC mortality between 1986 and 2001 [27,28]. The CC mortality rate in Mexico has also been falling since the mid-1980s, which is likely to be due to an increase in screening coverage. However, Latin American countries suffer a lack of standardisation of reporting with poor quality assurance and low coverage of women in rural areas [10]. But economic evaluation can provide a basis for prioritizing health interventions and prevention strategies.

2. Materials and methods

A Markov cohort model has been selected as the modelling tool, with transition probabilities in 1-year cycles between different health states describing the natural history from HPV infection to cancer and including the CC screening program in place [29–32]. The model is developed in Microsoft® Excel and is referenced to the more comprehensive model published by Goldie et al. [17]. The outputs of the models have been compared in a few countries worldwide and report comparable results [29,31,32].

In this health state transition modelling framework a female birth cohort of 11 years of age is allocated and reallocated every subsequent year between 12 different, mutually exclusive health states over time until everyone in the cohort has died (see Fig. 1). Values are assigned to each health state to reflect the cost and utility of spending one cycle in that state. The outcomes will therefore vary according to the length of time spent in each health state. The model shows the cohort's entire lifetime as a time horizon comparing two different intervention strategies. One strategy represents the current screening program (reference scenario), and the second strategy the current screening program with vaccination at 12 years of age. To reflect the present situation in each country we incorporated local epidemiological data, costs of national screening programs, and characteristics of treatment guidelines for

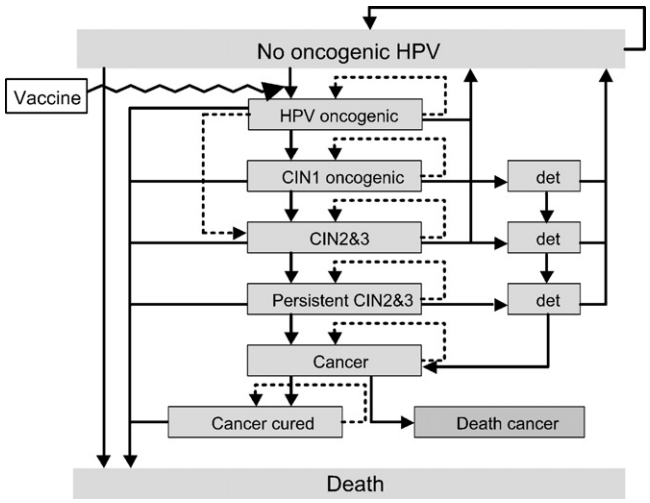

Fig. 1. Markov model framework. The filled boxes represent the possible health states that each woman would be assigned in one cycle. No oncogenic HPV: without oncogenic HPV infection; oncogenic HPV: persistent oncogenic HPV infection; CIN 1 oncogenic: cervical intraepithelial neoplasia (CIN) stage 1; CIN 2&3: CIN stages 2 and 3; persistent CIN 2&3: pre-invasive stage (carcinoma in situ); cancer: cervical cancer; cancer cured: cervical cancer remission; death cancer: death from cervical cancer; death: death from all other causes; det: women with disease detected through screening (same pathways but different probabilities). Solid arrows represent transition probabilities between health states (and direction). Broken arrows represent the probability of continuing in the same health state in the next cycle. When it is present, vaccination modifies the no oncogenic HPV—oncogenic HPV transition probability.

HPV-related lesions, among others. The model essentially considers the perspective of the health care payer for direct medical costs. All input data, as well as the model structure, were subjected to expert review in each country.

Due to lack of local data in the five countries analyzed we used probabilities for HPV and cervical intraepithelial neoplasia (CIN) natural progression and regression reported in the literature and adjusted to one cycle (1 year) transition rates (see Appendix B). The same values were used for all countries assuming the natural evolution of the disease is universal.

However the model has country-specific demographic and epidemiological data to reflect each country's socio-demographic specificities such as the population size of 11-year old girls, age-specific oncogenic HPV incidence rates, age-specific mortality rates, age-specific CC death rates, and the prevalence of HPV 16, 18, 31 and 45 in invasive CC. Country-specific data were identified by reviewing different sources of information such as scientific publications and local statistics.

Age-specific oncogenic HPV incidence was modelled using local prevalence data. The risk of infection with oncogenic HPV for a cohort was estimated from the age-specific prevalence of oncogenic HPV within each country. An annual regression rate of 50% was assumed for HPV infections to estimate incidence data from prevalence data [33,34].

CC mortality rate (i.e. lethality) was calculated from GLOBOCAN 2002 [6] for each country, using the following formula:

$$\text{Lethality}_i = \frac{\text{CC deaths}_i}{\text{Total CC}_i}; \quad (1)$$

where Lethality_i = CC mortality rate in women with CC at age i; CC deaths_i = number of deaths of patients with CC at age i; Total CC_i = prevalent CC cases at age i (i.e. total number of patients with CC diagnosed during the previous 5 years who survived up to age i). Finally, data were smoothed for inclusion into the model (see Appendix B).